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EXAMINER	
MUMMERT, STEPHANIE KANE	
ART UNIT	PAPER NUMBER
1637	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/24/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/802,162	GETTS, ROBERT	
	Examiner	Art Unit	
	Stephanie K. Mummert, Ph.D.	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 September 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 September 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The examiner of record has changed. Please address future correspondence to Stephanie Mummert, whose contact information is included at the end of this communication.

Applicant's amendment filed on September 12, 2006 is acknowledged and has been entered. Claims 4, 19, 24 and 27-34 have been amended. Claims 1-42 are pending.

Claims 1-42 are discussed in this Office action.

All of the amendments and arguments have been thoroughly reviewed and considered but are not found persuasive for the reasons discussed below. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

This action is made FINAL as necessitated by applicant's amendment to the claims.

Previous Rejections

The objection to the Specification is withdrawn in view of Applicant's amendment to the drawings, including corresponding sequence identifying SEQ ID NOs.

The rejection of claims 1-42 under 35 U.S.C. 103(a) as being unpatentable over Dellinger in combination with Nielsen and/or Lane are withdrawn in view of applicant's amendment to the claims.

NEW REJECTIONS

Claim Objection

1. Claim 9 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. As currently recited the method of claim 9 depends from the method of claim 9.

Priority

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 60/187681, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. Specifically, for claims 28, 30, 32 and 34, the prior filed provisional application does not disclose the use of at least three different capture sequences as part of multiple channel analysis. Instead, the specification of the prior filed application only makes reference to "3DNA™ expression array reagents are available with either Cy3™ or

Cy5™ attached to the 3DNA™ molecule, making possible either single or dual channel detection in array experiments" (p. 1 of prior filed application). Therefore, due to the failure to provide adequate support for these claims, as currently amended, claims 28, 30, 32 and 34 are being afforded the effective filing date of the instant application, filed March 8, 2001.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 1-2, 5-15, 18, 20-22 and 35-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sampson et al. (GB 2332516; June 1999 publication) in view of Nilsen et al. (USPN. 5, 487,973; January 1996). Sampson teaches a method for the amplification of the signal of target sequences using a bidirectional primer and cDNA synthesis (Abstract).

With regard to claim 1, Sampson teaches a method for detection and assay on a microarray, comprising:

a) taking a microarray having thereon a plurality of features each comprising a first particular first nucleotide sequence (p. 9, lines 28 to p. 10, line 3, where tagged cDNA is hybridized to the surface of an array; p. 1, lines 10-15, p. 7, lines 19-23 and p. 16, lines 16-18, where the type of array is described as comprising nucleic acid),

b) taking a first component comprising cDNA reagents having a capture sequence (Figure 1, where cDNA is generated that comprises a 3' sequence that provides a 'capture' sequence; p. 9 lines 4-26, specifically steps 1 and 2, where the target mRNA is transcribed into cDNA using a bidirectional primer); and

c) wherein said cDNA reagents comprise a plurality of different nucleotide sequences, and wherein said capture sequence of cDNA reagents is a common sequence among said cDNA reagents, said common sequence being complementary to the nucleotide sequence of said aptamer or signal amplification unit (Figure 1, where the bidirectional primer comprises a sequence that is common to all cDNA targets and which is complementary to the circular probe which generates a repeated signal amplification sequence with fluorescent labels or, see p. 11, lines 21-22, where it is contemplated that second half of the bidirectional primer is an aptamer for the purpose of generating signal amplification of the target w/ the aptamer attached; or see p. 16, lines 7-10, where signal amplification may be achieved by hybridizing a fluorescently tagged probe to the defined sequence added by the bidirectional primer);

d) mixing said first and second components at a temperature and for a time sufficient to enable said first component to bind to said second component (Figure 1, step 2, where the cDNA reagent is combined with a second component); and

e) incubating this mixture with said microarray to enable the first nucleotide sequences to bind to said first component, wherein said binding results in the generation of a hybridization pattern on the microarray (p. 9, lines 28 to p. 10, line 9, where tagged cDNA is hybridized to the surface of an array and the signal generated is detected).

With regard to claim 2, Sampson teaches the method of claim 1, wherein said cDNA reagents are obtained from mRNA of a target sample and further comprising the step of forming the first component comprising the cDNA reagent by contacting the mRNA with a quantity of a RT primer having the capture sequence, and with a reverse transcriptase, and nucleotide under conditions sufficient for initiating reverse transcription of the mRNA into said cDNA reagents (Figure 1, where cDNA is generated that comprises a 3' sequence that provides a 'capture' sequence; p. 9 lines 4-26, specifically steps 1 and 2, where the target mRNA is transcribed into cDNA using a bidirectional primer).

With regard to claim 10, Sampson teaches an embodiment of claim 1, further comprising scanning the microarray for detecting the detectable signal and the hybridization pattern generated (p. 9, lines 28 to p. 10, line 9, where tagged cDNA is hybridized to the surface of an array and the signal generated is detected).

With regard to claim 18, Sampson teaches a method for detection and assay on a microarray, said method comprising the steps of:

1) incubating a mixture including:

a first component comprising cDNA reagents having capture sequence (Figure 1, where the bidirectional primer comprises a sequence that is common to all cDNA targets and which is complementary to the circular probe which generates a repeated signal amplification sequence with fluorescent labels or, see p. 11, lines 21-22, where it is contemplated that second half of the bidirectional primer is an aptamer for the purpose of generating signal amplification of the target w/ the aptamer attached; or see p. 16, lines 7-10, where signal amplification may be achieved by

hybridizing a fluorescently tagged probe to the defined sequence added by the bidirectional primer); and

a second component comprising an aptamer/signal amplification region having a second nucleotide sequence (Figure 1, step 2, where the cDNA reagent is combined with a second component, wherein this component is depicted as a circular probe which generates a repeated signal amplification sequence with fluorescent labels; p. 11, lines 21-22, it is also contemplated that the signal amplification is generated through contact with an aptamer; or see p. 16, lines 7-10, where signal amplification may be achieved by hybridizing a fluorescently tagged probe to the defined sequence added by the bidirectional primer);

wherein said cDNA reagents comprise a plurality of different nucleotide sequence and wherein said capture sequence of said cDNA reagents is a common sequence among said cDNA reagents, said common sequence being complementary to said second nucleotide sequence of said aptamer, said capture sequence being used for binding said aptamers/signal amplification regions to said cDNA reagents (Figure 1, where the bidirectional primer comprises a sequence that is common to all cDNA targets and which is complementary to the circular probe or, see p. 11, lines 21-22, where it is contemplated that second half of the bidirectional primer is an aptamer for the purpose of generating signal amplification of the target w/ the aptamer attached; or see p. 16, lines 7-10, where signal amplification may be achieved by hybridizing a fluorescently tagged probe to the defined sequence added by the bidirectional primer);

2) contacting a microarray having thereon a plurality of features each comprising a particular first nucleotide sequence with said mixture (p. 9, lines 28 to p. 10, line 9, where tagged cDNA is hybridized to the surface of an array and the signal generated is detected); and

3) incubating said microarray and said prehybridized cDNA-signal amplification complex at a second temperature and for a time sufficient to induce said prehybridized cDNA-aptamer/signal amplification complex to bind to said first nucleotide sequence, wherein such binding results in the generation of a hybridization pattern on said microarray (p. 9, lines 28 to p. 10, line 9, where tagged cDNA is hybridized to the surface of an array and the signal generated is detected).

With regard to claim 20, Sampson teaches an embodiment of claim 1, wherein said mixing of said first and second components is conducted on said microarray (p. 10, lines 10-16, where the order of steps can be varied and may included hybridization of the 1st and second components before hybridization to the array, or after).

With regard to claim 21, Sampson teaches an embodiment of claim 1, wherein said mixing of said first and second components is conducted off of said microarray (p. 10, lines 10-16, where the order of steps can be varied and may included hybridization of the 1st and second components before hybridization to the array, or after).

With regard to claim 22, Sampson teaches an embodiment of claim 18, wherein said cDNA reagents are obtained from mRNA of a target sample and further comprising the step of forming the first component comprising the cDNA reagents by contacting the mRNA with a quantity of a RT primer having the capture sequence and with a reverse transcriptase, and nucleotide under conditions sufficient for initiating reverse transcription of the mRNA into cDNA reagents (Figure 1, where cDNA is generated that comprises a 3' sequence that provides a 'capture' sequence; p. 9 lines 4-26, specifically steps 1 and 2, where the target mRNA is transcribed into cDNA using a bidirectional primer).

With regard to claim 35 and 37, Sampson teaches an embodiment of claim 1 and 18, wherein said capture sequence comprises more than one type of base (p. 9, lines 23-26).

With regard to claim 36 and 38, Sampson teaches an embodiment of claim 1 and 18, wherein said capture sequence comprises adenine, guanine, cytosine and thymine bases (p. 9, lines 23-26).

With regard to claim 39-40, Sampson teaches an embodiment of claim 1 and 18, wherein said method is used for expression analysis (p. 1, lines 12-15, where arrays are useful for expression analysis).

However, Sampson did not teach use of dendrimer nucleotide sequences comprising at least one first arm comprising a label and at least one second arm having a second nucleotide sequence.

Nilsen et al. teach a method of claims 1-26 and 35-42, for detecting a specific nucleic acid in a target sample using a dendrimeric probe wherein Nilsen et al. teach that the method comprises (i) contacting a bead having specific probe sequences with a mixture containing a first component comprising labeled target nucleic acid (DNA or RNA) having a capture sequence and a second component comprising a dendrimer having at least one arm with a nucleotide sequence complementary to the capture sequence of the first component (see column 14, lines 30-35, column 15, lines 37-63); (ii) mixing the first and second components at a temperature to form a bridge between the two components to enable the cross-linking of first component to the second (see column 16, lines 8-11); and incubating the bound mixture with the said bead and detecting signal as an indication of the binding of the target sequence to the specific probe sequence on the bead (see column 16, lines 12-67, column 18, lines 27-51). Nilsen et al. also teach that the

method comprises annealing times ranging from 8 minutes (see column 20, lines 24-44) to overnight to 2-6 weeks (see column 3, lines 49-60); detection of hybridization pattern includes detecting the detectable signal (see column 20, lines 38-40); the method comprises hybridization buffer (see column 19, lines 14-26); the unbound dendrimers were removed by a washing step (see column20, lines 35-37); and the isolation of nucleic acid includes spin column (see column20, lines 17-19).

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made, to modify a method for using microarray hybridization as taught by Sampson with a method for detecting a nucleic acid sequence using dendrimer as taught by Nilsen et al. to achieve expected advantage of developing an enhanced sensitivity of detecting a target nucleic acid because Nilsen et al. states that "background noise could be generated in conventional assay not only from binding to a solid support, but also from binding of the probe to nonhomologous DNA sequences. An open branching of a dendrimeric DNA have many degrees of freedom in their movement relative to each other and have a high avidity for DNA that is complementary to the non-annealed single stranded sequences (see column 18, lines 14-26, column 7, lines 14-19). Furthermore, the method taught by Sampson is directed specifically to "a method of amplifying the signal of a target nucleic acid sequence" (p. 4, lines 27-28) and therefore, the two methods are directed to different methods of achieving signal amplification of target nucleic acid sequences using fluorescence. Therefore, an ordinary practitioner would have been motivated to combine the method of Sampson with the step of adding dendrimeric probe as taught by Nilsen et al. in order to achieve the expected advantage of developing a sensitive method for detecting a target nucleic acid because the addition of the

limitation as taught by Sampson would reduce non-specific binding and reduce background noise and enhance specific hybridization signal.

3. Claims 3-4, 16-17 and 23-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sampson et al. (GB 2332516; June 1999 publication) in view of Nilsen et al. (USPN. 5, 487,973; January 1996) as applied to claims 1-2, 5-15, 18-22 and 35-42 above, and further in view of Combates et al. (US Patent 6,045,998; April 2000).

With regard to claim 16-17 and 25-26, Nilsen teaches an embodiment of claim 3 and 23, wherein the purging step further comprises the use of a hybridization chamber or station (col. 20, lines 20-33).

However, neither Nilsen nor Sampson teaches the use of a spin column to remove unhybridized RT primer. Combates teaches the exclusion of excess RT primer prior to the use of cDNA in downstream applications.

With regard to claim 3 and 23, Combates teaches an embodiment of claim 2 and 22 further comprising the step of purging excess unhybridized RT primer from said first component prior to incubation of said mixture (col. 9, lines 33-38, where excess oligo-d(T), which is used as an RT primer at col. 9, lines 1-4, is removed by chromatography on a spin column).

With regard to claim 4, 19 and 24, Combates teaches an embodiment of claim 3 and 23, wherein the purging step further comprises the step of passing the first component through a spin column media to remove excess RT primer (col. 9, lines 33-38, where excess oligo-d(T), which is used as an RT primer at col. 9, lines 1-4, is removed by chromatography on a spin column).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have extended the teachings of Sampson to incorporate the step of removing excess reverse transcriptase primer as taught by Combates to arrive at the claimed invention with a reasonable expectation for success. As taught by Combates, "contaminating oligo(dT) primer was removed by chromatography on a spin column" (col. 9, lines 33-38) prior to further downstream processing including amplification of the cDNA and electrophoresis. Therefore, considering the teachings of Combates where excess RT primer was removed prior to further analysis of the synthesized cDNA and considering the focal role the bifunctional RT primer plays in the method taught by Sampson in view of Nilsen, one of ordinary skill in the art at the time the invention was made would have been motivated to include the step of RT primer removal taught by Combates into the method of signal amplification taught by Sampson and Nilsen to arrive at the claimed invention with a reasonable expectation for success.

It is noted that these claims were previously rejected and the rejection was inadvertently omitted from the previously mailed office action. Based upon applicant's response, the typographical error did not result in confusion and the claims remain rejected. The new grounds of rejection is necessitated by Applicant's amendment to the claims.

4. Claims 27-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sampson et al. (GB 2332516; June 1999 publication) in view of Nilsen et al. (USPN. 5, 487,973; January 1996) as applied to claims 1-2, 5-15, 18-22 and 35-42 above, and further in view of Brenner et al. (US Patent 5,846,719; December 1998).

With regard to claims 27-34, Sampson teaches a method which comprises dual or multi-channel analysis (p. 10, lines 6-9, where the tags incorporated into the signal amplification sequence are fluorescent moieties that may be detected by monitoring the fluorescence emission at defined sets or ranges of wavelengths).

With regard to claim 27, 29, 31 and 33, Brenner teaches an embodiment of claim 1-2, 18 and 22, such that said analysis uses two different capture sequences (col. 11, line 61 to col. 12, line 20, where oligonucleotide tags preferably range in length from 18-40 nucleotides and preferably contain at least 100 members, which is more than 2 different capture sequences).

With regard to claim 28, 30, 32 and 34, Brenner teaches an embodiment of claim 1-2, 18 and 22, such that said analysis uses at least three different capture sequences (col. 11, line 61 to col. 12, line 20, where oligonucleotide tags preferably range in length from 18-40 nucleotides and preferably contain at least 100 members, which is more than 3 different capture sequences).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have incorporate the multitude of oligonucleotide tags taught by Brenner into the method of signal amplification taught by Sampson and Nilsen to arrive at the claimed invention with a reasonable expectation for success. Brenner addresses a need in the art by providing, "an oligonucleotide-based tagging system which provided a large repertoire or tags, but which also minimized the occurrence of false positive and false negative signals without the need to employ special reagents for altering natural base pairing and base stacking free energy differences. Such a tagging system would find applications in many areas, including construction and use of combinatorial chemical libraries, large-scale mapping and sequencing of DNA, genetic identification, medical diagnostics and the like". Brenner also teaches how this

variety of oligonucleotide tags, may be synthesized, including "oligonucleotide tags of the invention are synthesized combinatorially out of subunits between three and six nucleotides in length and selected from the same minimally cross-hybridizing set" (col. 8, lines 50-53). Finally, Brenner notes that "the invention provides a method of labeling and sorting molecules, particularly polynucleotides by the use of oligonucleotide tags" (col. 7, lines 42-44). Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to adjust the method taught by Sampson and Nilsen to incorporate the variety of additional oligonucleotide tag sequences taught by Brenner into to arrive at the claimed invention with a reasonable expectation for success.

Response to arguments:

5. Applicant's arguments with respect to claims 1-42 have been considered but are moot in view of the new ground(s) of rejection necessitated by Applicant's amendment to the claims.

6. With regard to the rejection under provisional double patenting, Applicant's arguments are fully considered and found unpersuasive because it is not the only remaining rejection in this application. As discussed above, the rejections under 35 U.S.C. 103(a) are still pending. Thus, the rejection under provisional double patenting is maintained until the issues are resolved.

Relevant Prior Art

7. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Wolber et al. (US Patent 6,235,483; May 2001) discloses methods and kits for labeling nucleic acids using tagged oligonucleotides (Abstract).

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephanie K. Mummert, Ph.D. whose telephone number is 571-272-8503. The examiner can normally be reached on M-F, 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Stephanie K Mummert, Ph.D.
Examiner
Art Unit 1637

JEFFREY FREDMAN
PRIMARY EXAMINER
1/4/07